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Short Reviw

Cognitive Dysfunctions in Inflammatory Bowel Disease and Irritable Bowel Syndrome

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Abstract

The aim of this paper is to summarize the current evidence on cognitive dysfunctions in adults with inflammatory bowel disease and inflammatory bowel syndrome.The online databases PubMed and PsycINFO were searched. All quantitative studies published in English found in the mentioned databases until December 2019 were included. Quantitative studies which did not include a control group, qualitative studies and case studies were excluded. We found seven papers about cognitive dysfunctions in IBD and IBS. Four of seven papers compare cognitive functions of patients with IBD and IBS. Three of seven studies assess cognitive functions in IBD. Three papers assessed memory, three papers studied selective attention and inhibition response, two papers assessed cognitive flexibility, one paper measured information processing speed, and one paper assessed verbal fluency.

***Keywords**: inflammatory bowel disease, inflammatory bowel syndrome; cognitive impairment, adults*

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Introduction

Inflammatory bowel disease (IBD) and irritable bowel syndrome(IBS) are two common and chronic gastrointestinal disorders that have some similarities. They have symptoms and signs similarities and pathophysiological similarities including increased gut permeability, brain-gut axis dysfunction and abnormal gut microbiota[1-2].

Brain morphological changes have been described in adults with IBD. Decreased grey matter volumes in dorsolateral prefrontal cortex and in anterior midcingulate cortex were observed in CD patients during remission (comparing with a control group). Furthermore, disease duration was negatively correlated with gray matter volume in subgenual anterior cingulate, posterior midcingulate cortex, ventral posterior cingulate and parahippocampal cortices[3]. Zikou et al[4]compare 18 IBD patients (mean aged 45.16years old) with 20 aged-matched control subjects using tract-based spatial statistics and voxel-based morphometry methods. They found larger number of whitematter hyperintensities and decreased axial diffusivity in the right corticospinal tract and in the right superior longitudinal fasciculus in IBD patients. In addition, they observed decreased grey matter volume in the fusiform, the inferior temporal gyrus, the right precentral gyrus, the right supplementary motor area, the right middle frontal gyrus and the left superior parietal gyrus in IBD patients.

The mechanisms underlying these anatomical changes have not been elucidated. Agostini et al[3] suggest that the overproduction of inflammatory mediators in CD may promote gray matter changes by inducing apoptosis. Furthermore, inflammatory signals from gut may reach cortical and subcortical areas via the brain gut axis. Zikou et al[4] proposed that the combination of central nervous system vasculitis, neurotoxicity by the cytokines and Wallerian degeneration might be responsible for matter hyperintensities, withe matter tract damage and gray matter atrophy in IBD patients. Furthermore, because brain and intestine are connected by neuronal, endocrine, immune and metabolic pathways, dysregulation in these pathways might contribute at least partially to cognitive dysfunctions (5).

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For example, if the composition of the intestinal microbiota changes, there will be changes in neuropeptides and neurotransmitters that might affect cognitive functions.

Considering the above mentioned (anatomical changes) and that anatomical changes are often associated with functional changes we could expect that adults with IBD have cognitive dysfunctions.

On behalf of IBS, Chen et al 2016[6] reported that IBS was associated with and increased risk of dementia in patients older than 50 years old. Authors suggest that activation of gut immune system, altered brain-gut interaction and dysbiosis may contribute to explain this association.

Considering the above mentioned (association between IBS and dementia) and that dementia usually involve a progressive cognitive decline, we could expect that adults with IBS have cognitive dysfunctions.

Due to IBD and IBS similarities (reported in bibliography), IBD and IBS might have also some similarities at cognitive level.

The aim of this review is to summarize the current evidence on cognitive dysfunctions in IBD and IBS.

Methods

The online databases PubMed and PsycINFO were searched using the main terms: IBD/IBS + cognition/cognitive impairment/cognitive function; inflammatory bowel disease/ inflammatory bowel syndrome + cognition/cognitive impairment/cognitive function.

All quantitative studies published in English found in the mentioned databases until September 2019 were included. Quantitative studies which did not include a control group, qualitative studies and case studies were excluded.

Results and future studies

We found seven papers about cognitive dysfunctions in IBD and IBS. Four of seven papers compare cognitive functions of patients with IBD and IBS.Three of seven studies assess cognitive functions in IBD.

As for neurocognitive process assessed, three papers assessed memory, three papers studied selective attention and inhibition response, two papersassessed cognitive flexibility,one paper measured information processing speed, and one paper assessed verbal fluency.

Studies reviewed include small samples and neuropsychological techniques used are heterogeneous. Despite this, in general, similarities were found in cognitive disturbances in IBD and IBS patients.

Concerning information processing speed,slow information processing speed have been reported in CD patients (comparing to controls). Furthermore, lower information processing speed was associated with higher serum C reactive protein levels[7]. This result suggests a relationship between a state of systemic inflammation and the velocity of information processing. If speed processing is slow, cognitive functions may be compromised. Slow information processing speed is usually associated with alterations in brain white matter[8]. Structural changes in white matter had been reported in IBD patients (they were mentioned in the introduction). These structural changes might affect information processing speed. Functional changes associated with structural changes in white matter might mediate the effect of structural damage on information processing speed. Future studies should explore furtherthe association between brain structuralalterations and cognitive dysfunctions and explore the relationship between inflammation markers/mediators and other cognitive dysfunctions besides information processing speed.

In relation to cognitive flexibility,cognitive flexibility dysfunctions have been reported in IBD and IBS patients [9-10]. This result could be attributed to damage in frontal regions, both reported in patients with IBDand IBS[3-4,10]. Performance in cognitive flexibility could be compromised by slow processing speed. Since processing speed and cognitive flexibility were studied in different papers, it is not possible to comment on this. Therefore, future studies might assess information processing speed, attention, memory, visuospatial skills, language, effective functions and social cognition, in all participants.

As for inhibition response and selective attention,two of three studies did not find dysfunctions in inhibition response and selective attention in IBD and IBS patients[11-12]. One of three studies[13] report poor performance in inhibition response and selective attention in IBD. This poor performance was explained by mood disturbance. However, poor performance in inhibition response and selective attention are still significant in CD patients without mood disturbance.This result could be attributed to the structural alterations reported in frontal and parietal lobes in IBD patients. Anxiety and depression are known to negatively affect cognitive functioning. Future studies may compare the cognitive functioning of patients with and without mood disturbances and explore if mood disturbance treatment improves cognitive performance. In addition, due to the relationship between inflammation and cognitive disorder on the one hand, and, between inflammation and mood disorders in on the other, it remains to study in depth the possible effect of inflammation on the cognitive functioning of patients with IBD and without mood disturbances.

Concerning memory, the reviewed studies[11-13] do not provide evidence of memory impairment in IBD patients. In contrast, IBS patients had a subtle episodic memory deficit[13].

Relating to verbal fluency, in one out of one paperauthors did not find verbal fluency deficits in CD patients[14]. During verbal fluency task IBD patients hadbi-hemispheric pattern activation. Future studies should include functional neuroimaging to explore if compensation mechanism by activating homologous areas is common in IBD patients in different tasks and / or if recruit nearby areas during performance tasks to achieve a performance comparable to control group.

One of seven papers compare cognitive performance between CD and UC patients[12]. Authors did not find statistically significant differences. Future studies should analyze if CD and UC patients have a different neuropsychological profile.

Conclusion

Most of the studies reviewed did not include enough patient medical information. Future neuropsychological studies in IBD patients may include information on the clinical status of the participants to explore whether there are relationships between IBD severity and cognitive dysfunctions, if treatments exert differential effects on cognition, and whether cognitive changes occur as the disease progresses.

Conflict of interest statement: The Author declares that there is no conflict of interest.

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